Dear editors and reviewers,

Thank you for your letter and for the reviewers’ comments on our manuscript entitled “Trigeminal extracranial radiofrequency combined with esketamine for patient-controlled intravenous analgesia in the treatment of refractory herpes zoster ophthalmicus: A case report”. We sincerely thank the editors and reviewers for their careful read and thoughtful comments on previous draft. Through the guidance of the editors and experts, we realized the shortcomings of the study and got some inspiration. Based on the comments we received, careful modifications have been made to the manuscript. Below is our point-by-point response to the reviewers’ comments.

If you have any further queries, please feel free to contact us.

Best Regards

Ming Yao

Reviewers’ comments:

Reviewer #1: The case report “Trigeminal extracranial radiofrequency combined with esketamine for patient-controlled intravenous analgesia in the treatment of refractory herpes zoster ophthalmicus: A case report” is well written though I have the following concerns:

• The title can be “Trigeminal extracranial thermocoagulation along with patient-controlled analgesia with esketamine for refractory post herpetic neuralgia after herpes zoster ophthalmicus: A case report”. According to the article, radiofrequency did not relieve the pain and thermocoagulation was done.

Response: We appreciate the reviewer positive suggestion of our case. We have changed the title of this case to “Trigeminal extracranial thermocoagulation along with patient-controlled analgesia with esketamine for refractory post herpetic neuralgia after herpes zoster ophthalmicus: A case report”.

• In the case report, the authors mention that the patient was hospitalized for 20 days but had pain for only 3 days? This should be clear…why the patient was hospitalized and when the pain started.
Response: Thank you very much for your valuable comments. In this case, patient chief complaint is “left frontal parietal herpes for 20 days with pain for 3 days”. The patient developed pain on the 17th day after ocular herpes zoster and was hospitalized because the pain did not relieved.

- What antiviral drug and how much was given to the patient.
  Response: The antiviral drugs taken by the patient was oral valaciclovir capsule (0.3g bid) and external application of acyclovir cream for one week. It has been described in detail on line 70-71 on page 3 of the article.

- Was the antiviral treatment started within 72 hours of the onset of disease?
  Response: Yes.

- Why no steroids were given to the patient, was it due to diabetes?
  Response: Because the patient has a history of diabetes, steroids were not use to in our case.

- Were tricyclic antidepressants tried? Was gabapentin or pregabpentin given at the beginning of the disease.
  Response: Tricyclic antidepressants were not used in this case. The patient was given gabapentin capsules (0.3 g bid), It has been described on line 90-91 on page 3 of the article.

- In history of past illness, the first sentence should be as follows: “The patient had a history of diabetes for more than 10 years and was being treated with Metformin.”
  Partial gastrectomy was done for what reason should be mentioned.
  Response: In this case, the patient underwent subtotal gastrectomy because of gastric cancer. Lines 79-80 on page 3 of the article have been changed.

- There is no need for titles for examination and history, instead one can just write:
  There was no significant family history and physical examination was normal. All laboratory investigations and imaging investigations were normal including the liver function. (typo error of “He” instead of “She”)
  Response: Thank you very much for your valuable comments. We have changed this section to "There was no significant family history and physical examination was
normal. All laboratory investigations and imaging investigations were normal including the liver function" and see lines 82-84 on page 3.

• The final diagnosis was Herpes zoster ophthalmicus or post heraptic neuralgia after HZO? The pain had started 17 days after HZO and full treatment with antivirals so post herpatic neuralgia should be considered.

Response: We appreciate the reviewer suggestion of this case. We have changed the final diagnosis to "Postherpetic neuralgia after herpes zoster ophthalmicus; Diabetes” and see lines 87 on page 3.

• Gabapentin, paracetamol and oxycodone wee started after 17days of HZO or at day 1 of HZO? This is not very clear.

Response: Gabapentin capsules and paracetamol oxycodone tablets was given on the 17 days after HZO.

• CT guided radiofrequency of trigeminal nerve is a “procedure” and not a “surgery”; so kindly remove the word “surgery” and “operation” and replace it with “procedure”

Response: Thank you for your valuable comments. We have replaced “surgery” and “operation” with “procedure”.

• Was fentanyl patch tried in this patient?

Response: The patient was not used fentanyl patch.

• The total dose of esketamine 192 mg to 240 mg/24-hour period is very high while the midazolam is very low (5 mg). The patient’s weight should be mentioned at the beginning of the case description.

Response: Thank you very much for your valuable comments. In this case, midazolam was used to relieve the patient's psychiatric symptoms, and no obvious adverse reactions were observed at the 5mg. In further clinical studies, it may be considered to adjust the dose of midazolam to find the best dose. We added the patient's height and weight on page 2, line 64.

• In the discussion section, do mention that 7% of patients suffer from post herpatic neuralgia after HZO which may last from 30 days to 6 months. Also, pain relief for HZO will not reduce the complications like keratitis and visual impairment. Antiviral treatment, steroids and anti-inflammatory drugs will prevent the complications.
Response: We appreciate the reviewer suggestion of our case. We have added this part in the discussion section, see page 5, line 132-134.

- For PCA, the parameter settings were 8mg/hour basal rate…the bolus dose was 10 mg or 10mg/hour? Also, in the discussion, do mention that the peak effect of ketamine is after 15 to 20 minutes and hence the lockout time was 30 minutes.

Response: We are very sorry for this mistake, we have changed the bolus dose to 10mg. Besides, “the peak effect of ketamine is after 15 to 20 minutes and hence the lockout time was set to 30 minutes” is added in the discussion section.

- This is just a case report, so avoid using sentences like “in this study…”…this is not a study. So just write, “in this case…” or “in this patient…”

Response: Thank you for your valuable comment. We have changed “this study” to “this case”. Thank you again for your time and effort on this manuscript.